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09/889,251	11/01/2001	Robert K. Naviaux	UCSD1140-1	9760

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EXAMINER

SPIVACK, PHYLLIS G

ART UNIT PAPER NUMBER


1614

DATE MAILED: 12/18/2002

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary

Application No. 09/889,251	Applicant(s) Naviaux
Examiner Phyllis G. Spivack	Art Unit 1614



- The MAILING DATE of this communication appears on the cover sheet with the correspondence address -

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136 (a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

- 1) Responsive to communication(s) filed on Jul 18, 2002
- 2a) This action is FINAL. 2b) This action is non-final.
- 3) Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11; 453 O.G. 213.

Disposition of Claims

- 4) Claim(s) 1-66 is/are pending in the application.
- 4a) Of the above, claim(s) 29-65 is/are withdrawn from consideration.
- 5) Claim(s) _____ is/are allowed.
- 6) Claim(s) 1-28 and 66 is/are rejected.
- 7) Claim(s) _____ is/are objected to.
- 8) Claims _____ are subject to restriction and/or election requirement.

Application Papers

- 9) The specification is objected to by the Examiner.
- 10) The drawing(s) filed on _____ is/are a) accepted or b) objected to by the Examiner.
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
- 11) The proposed drawing correction filed on _____ is: a) approved b) disapproved by the Examiner.
If approved, corrected drawings are required in reply to this Office action.
- 12) The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

- 13) Acknowledgement is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
a) All b) Some* c) None of:
1. Certified copies of the priority documents have been received.
2. Certified copies of the priority documents have been received in Application No. _____
3. Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).
*See the attached detailed Office action for a list of the certified copies not received.
- 14) Acknowledgement is made of a claim for domestic priority under 35 U.S.C. § 119(e).
a) The translation of the foreign language provisional application has been received.
- 15) Acknowledgement is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

- 1) Notice of References Cited (PTO-892) 4) Interview Summary (PTO-413) Paper No(s). _____
- 2) Notice of Draftsperson's Patent Drawing Review (PTO-948) 5) Notice of Informal Patent Application (PTO-152)
- 3) Information Disclosure Statement(s) (PTO-1449) Paper No(s). 11 6) Other:

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Applicant's Preliminary Amendment, Paper No. 7, filed May 3, 2002 after the first Office Action mailed April 15, 2002, is acknowledged.

A Request for an Interference under 37 CFR 1.604 and an Amendment filed July 3, 2002, Paper No. 8, are further acknowledged. The Amendment presents new claims 28-65. On July 3, 2002, a Declaration by Robert K. Naviaux, Paper No. 9, was filed.

It is noted that among the three applications cited by Applicant in the request for an Interference, S.N. 09/930494 and S.N. 09/838136 have not yet received a first Action on the Merits. The remaining application, S.N. 09/144096, has issued as U.S. Patent 6,472,378 and recites only compound claims. The request for an interference is held in abeyance until an indication of allowable subject matter has been made on the record. A showing under 37 CFR 1.608(b) will be required.

An Amendment and Information Disclosure Statement, Paper Nos. 10 and 11, respectively, filed July 18, 2002, are further acknowledged. The references have been reviewed to the extent each is provided. New claim 66 is presented. Accordingly, claims 1-66 are now under consideration.

Newly submitted claims 29-65 are directed to inventions that are independent or distinct from the invention originally claimed for the following reasons: Methods for treating or preventing pathophysiological consequences of mitochondrial respiratory chain dysfunction, and, for treating developmental delay in cognitive, motor, language, executive function or social skills represent distinct subject matter from the originally claimed methods for the treatment of a mitochondrial disorder and reducing one or more

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symptoms associated with a mitochondrial disorder. New issues would be raised.

Further search is required.

Since Applicant has received an Action on the merits for the originally presentation for prosecution on the merits. Accordingly, claims 29-65 are withdrawn from consideration as being directed to a non-elected invention. See 37 CFR 1.142(b) and MPEP § 821.03.

In the last Office Action Claims 1-25 and 27 were rejected under 35 U.S.C. 112, second paragraph, as being indefinite with respect to the limitations "carbonyl derivative of an amino acid" in claim 4 and "carbonyl derivative of a dicarboxylic acid" in claim 5. Claims 4 and 5 were additionally rejected under 35 U.S.C. 112, first paragraph, as the claimed invention was not described in clear, concise and exact terms as to enable any person skilled in the art to make and use the invention with respect to both "a carbonyl derivative of an amino acid" and "a carbonyl derivative of a dicarboxylic acid".

The recitation "derivative" does not appear in claim 1, from which claims 4 and 5 depend. It is suggested the recitations -- the carbonyl moiety of an amino acid selected from the group... -- in claim 4 and -- the carbonyl moiety of a dicarboxylic acid -- in claim 5 are considered.

Following the amendments to claims 1 and 25, the rejection directed to lack of clarity concerning substituents is withdrawn. The definitions for the R₃, R₄ and R₅ terms are clear. Further, upon reconsideration it is clear CX₂ and CX₃ refer to a methylene unit and a methyl group, respectively. The X term is clearly defined.

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The rejection is maintained under 35 U.S.C. 112, second paragraph, only with respect to claims 4 and 5. The rejections of other claims under 35 U.S.C. 112, second paragraph, and the rejections of record under 35 U.S.C. 112, first paragraph, are withdrawn.

In the last Office Action claims 1, 7, 25 and 27 were rejected under 35 U.S.C. 102(b) as being anticipated by Isono et al., JP 53056690. It was asserted Isono teaches the administration of a compound of instant Formula I to treat angina, a symptom of a mitochondrial disorder, and to treat a hormone imbalance, which may relate to a mitochondrial disorder. Further, claims 1-7 and 25-27 were rejected under 35 U.S.C. 102(e) as being anticipated by Von Borstel et al., U.S. Patent 6,258,795. It was asserted Von Borstel teaches the administration of compounds of formula II and formula III to treat mitochondrial disorders or symptoms associated with mitochondrial disorders.

Applicant argues both of the cited reference are silent with respect to treating mitochondrial disorders.

Applicant's arguments have been carefully considered but are not found persuasive. The rejections are repeated for the reasons of record and are presently extended to include new claims 28 and 66. It is noted the present invention provides an understanding of the connection between mitochondrial disorders and the manifestation of disease states caused thereby. It is further recognized the references fail to recite the language "treatment of a mitochondrial disorder". However, the manifestation of a particular disease state through mitochondrial dysfunction is an inherent mechanism.

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Accordingly, treating angina, for example, is a treatment of mitochondrial disorder. *Ex parte Novitski*, 26 USPQ 2d 1389 (BOPA 1993) illustrates anticipation as a result of inherent use absent a haec verba recitation for such utility. In the instant application, as in *Ex parte Novitski*, the claims are directed to treating a mitochondrial disorder with well-known compounds. Administering compounds that inherently possess a utility anticipates claims directed to such use. Arguments that such inherent activity is not set forth haec verba are not probative. Prior use for treating angina, for example, clearly anticipates treating a mitochondrial disorder, absent limitations distancing the claims from the inherent anticipated use.

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

A person shall be entitled to a patent unless –

(a) the invention was known or used by others in this country, or patented or described in a printed publication in this or a foreign country, before the invention thereof by the applicant for a patent.

Claims 1-28 and 66 are rejected under 35 U.S.C. 102(a) as being anticipated by Naviaux et al, "Mitochondrial Dysfunction in Human Pathology" meeting in Melbourne, Australia.

Naviaux teaches the administration of triacetyluridime, the compound of claims 2 and 26, for the treatment of various mitochondrial disorders wherein the mitochondrial disorder comprises a deficiency in pyrimidine synthesis that results from a deficiency of the enzyme dihydroorotete dehydrogenates. Treatment is directed to disease^S of various organ systems.

(e) the invention was described in a patent granted on an application for patent by another filed in the United States before the invention thereof by the applicant for patent, or on an international application

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by another who has fulfilled the requirements of paragraphs (1), (2), and (4) of section 371(c) of this title before the invention thereof by the applicant for patent.

The changes made to 35 U.S.C. 102(e) by the American Inventors Protection Act of 1999 (AIPA) do not apply to the examination of this application as the application being examined was not (1) filed on or after November 29, 2000, or (2) voluntarily published under 35 U.S.C. 122(b). Therefore, this application is examined under 35 U.S.C. 102(e) prior to the amendment by the AIPA (pre-AIPA 35 U.S.C. 102(e)).

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repositioned
Claims 1-28 and 66 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention. In the present case the breadth of the claims with respect to treating a mitochondrial disorder is extremely broad. Little is known about the etiology and the pathophysiology of the various conditions and disease states specifically recited in dependent claim 7 and generally encompassed in independent claims 1, 2, 25 and 26. The level of ordinary skill in the art and the level of predictability in the art are minimal, to which the state of the art attests. The various Examples disclosed on pages 14-19 do not in all cases correlate with mitochondrial dysfunction. Undue experimentation would be required to practice the claimed methods of use. Insufficient guidance is provided by the specification to support the extremely broad claims. The determination of what constitutes undue experimentation requires the application of a standard of reasonableness.

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Claims 1-28 and 66 are rejected under 35 U.S.C. 102(e) as being anticipated by von Borstel et al., U.S. 6,472,378.

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Von Borstel teaches the administration of acyl derivatives of uridine and cytidine, including 2', 3', 5'-tri-O-acetyluridine to treat various mitochondrial disorders.

→ Loffler et al., Not. Cell Biochem., is cited to show further the state of the art with respect to the suggested treatment of mitochondrial disorders through uridine administration. See page 128.

No claim is allowed.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Phyllis Spivack whose telephone number is (703) 308-4703. The examiner can normally be reached on Monday to Friday from 9:00 AM to 5:00 PM.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Marianne Seidel can be reached on (703) 308-4725. The fax phone numbers for the organization where this application or proceeding is assigned are (703) 308-4556 for regular communications and (703) 308-3992 for After Final communications.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is (703) 308-1235.

Spivack/LR
November 19, 2002

Phyllis Spivack

**PHYLLIS SPIVACK
PRIMARY EXAMINER**